REMARKS

Claims 1-2 and 7-25 are pending in this application. The Examiner has maintained the rejection of claim 1 under 35 U.S.C. §112, second paragraph, and the art rejection of claims 1-2 and 9-22 under U.S.C. § 102(b) in light of Griffiths *et al.* (Scale-Up Suspension and Anchorage-Dependent Animal Cells, *in* Basic Cell Culture Protocols, Ed. Pollard *et al.*, Humana Press Inc., 1997, pp. 59-75; hereafter "Griffiths"). The Examiner has raised a new ground of rejection of claims 1-2 and 9-22 under 35 U.S.C. §103 over the combination of Griffiths and Pollard (Basic Cell Culture, *in* Basic Cell Culture Protocols, Ed. Pollard *et al.*, Humana Press Inc., 1997, pp. 1-11; hereafter "Pollard"). Applicant respectfully traverses each of these grounds of rejection.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has maintained the rejection of claim 1 under 35 U.S.C. §112, second paragraph, as to the term "biologicals." The Examiner continues to allege that Applicant has failed to particularly point out the metes and bounds of the term "biologicals." Office action at page 2. Applicant maintains that the objected-to term is specifically defined in the specification as:

> "any substance or organism which can be produced from a cell culture. Examples of 'biologicals' are viruses and proteins such as enzymes."

Specification at page 2, lines 34-36. Applicant also submits that one skilled in the art would fully understand the scope of the term as used in the claims in view of the definition given in the specification. The term "biologicals" is a generic, art-recognized

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term, that when taken in the context of the definition in the specification, would clearly identify to the skilled artisan the scope of the claimed invention. The Examiner had asked earlier whether, for example, CO_2 would be considered a biological. *See* Office action of February 12, 2001. According to the definition of a biological in the specification, as quoted above, CO_2 would clearly not be encompassed by the term. One skilled in the art would not have any doubt as to how to answer the Examiner's question.

Applicant also contends that the definition of the term "biological" can be readily found in dictionaries or encyclopedias as evidence that one skilled in the art would know or would have reason to know of the term's standard meaning. A sample of definitions are provided below.

> "A medicinal product that is derived from biological sources." Random House Webster's College Dictionary, New York, 1999, page 135.
>
> "A drug or medicinal preparation obtained from animal tissue or some other organic source." Funk & Wagnalls Standard College Dictionary, New York, 1963, page 141.
>
> "Medicinal preparations made from living organisms and their products, including serums, vaccines, antigens, antitoxins, etc." Dorland's Illustrated Medical Dictionary, Philadelphia, PA, 1974, page 169.

Accordingly, Applicant continues to submit that this reason for rejection is improper and should be withdrawn.

The Examiner also rejected claim 1 under the second paragraph of section 112, suggesting that the metes and bounds of "a desired cell volume" are not defined.

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Furthermore, the Examiner argues that the claim should point out the range of the cell volume that is intended in the claim. Office action at page 2.

As noted in the Response filed June 12, 2001, at pages 4-5, the desired cell volume is exemplified in the specification. At least two examples of desired cell volumes can be found in the specification, i.e. 5×10^6 cells/ml (Example 1) and 2.8×10^6 cells/ml (Example 7). One of skill in the art would be able to modify the Examples of the specification to prepare their desired cell volume in view of the indicated subsequent use. One would generate the number of cells required to produce efficiently, within a given period of time, both a new preproduction batch and the desired amount of biological in the production batch.

Because the specification adequately defines specific cell volumes that can be obtained with the instant invention and because it would be obvious for one to modify these volumes according to his own needs, Applicant contends that the requirements of § 112, second paragraph have been satisfied. Applicant respectfully requests that this rejection therefore be withdrawn.

Rejection under 35 U.S.C. § 102(b)

The Examiner has again rejected claims 1-2 and 9-22 under 35 U.S.C. § 102(b) over Griffiths. Office Action at pages 2-3. Specifically, the Examiner contends that Griffiths "teaches all principles and every general step of scale-up culture." Applicant

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respectfully disagrees. The pertinent methods disclosed in Griffiths only disclose the following:

Item 3.1.2. teaches a culture procedure for suspension cells, wherein the cells are "harvested or maintained with medium changes" to avoid death. Griffiths at page 63, lines 20-21.

Item 3.2.1.1. teaches a method of roller culture, wherein the cells are "harvested, diluted in fresh medium and serum, and passaged on." Griffiths at page 67, lines 20-21.

Item 3.2.1.2.1. teaches a procedure for growing cells on immobilized beds. Griffiths states that the method is "more suitable for harvesting a secreted cell product over a long period of time, rather than acting as a source of cells." Griffiths at page 69, lines 32-33.

Item 3.2.1.3.2. teaches a procedure for growing cells as a microcarrier culture, wherein "cells can be harvested." Griffiths at page 71, line 5.

Item 3.3.1. teaches a glass sphere culture system that is "very suitable for secreted cell products and can be operated as a continuous perfusion process for many months." Griffiths at page 71, lines 35-36. The method also teaches that all cells can be harvested when the glucose concentration drops below 1.5 mg/ml. Griffiths at page 73, line 7-8.

Item 3.3.2. teaches a fluidized bed culture system wherein the cells can be grown and harvested. Griffiths at page 73, second line from the bottom.

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As shown in this systematic review, at no time does Griffiths teach a "repeated discontinuous process," as claimed in the present application. A "repeated discontinuous process" is a method in which cells are split into two populations: one portion of the produced cells of each generation cycle is used as seed cells for the next generation, while the other portion is discontinued from the propagation process and can be used for biological purposes. Because Griffiths does not teach each and every element of the instant invention, and certainly the Examiner has not demonstrated to the contrary, Applicant respectfully requests that the rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

The Examiner has raised a new ground of rejection of claims 1-2 and 7-25 under 35 U.S.C. § 103(a), contending that the instant invention is unpatentable over the combination of Griffiths and Pollard for the reasons found at pages 3-4 of the Office action.

As explained above, Griffiths fails to teach a "repeated discontinuous process" in which a first portion of cells of the preproduction batch is used for the preparation of at lease one production batch, and the remaining cells of the preproduction batch are used as seed cells for the preparation of at least one subsequent preproduction batch, as required by the instant invention. The Examiner states that "a repeated discontinuous process is just a design choice based on Griffiths." Office action at page 4, lines 22-23. Applicant fully disagrees as Griffiths does not contemplate a repeated discontinuous

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process. Further, the Examiner has not pointed to any teaching in Griffiths, or in the knowledge of the art that would lead one to such a "design" choice.

This shortcoming is not remedied by Pollard. Sections 3.1.1. and 3.1.2. of the Pollard reference merely disclose that cells can be harvested and frozen, while section 3.2. merely teaches a method for harvesting cells and transferring them to the next subculture. Pollard at pages 2-5. Because the combined teachings of the references do not and cannot result in the claimed invention, Applicant respectfully requests that the rejection be withdrawn.

Furthermore, and paramount, the Examiner has failed to demonstrate that one skilled in the art would be motivated to combine the Griffiths and Pollard references. Even if, *arguendo*, the combined references did provide all of the elements of the instant invention, the Examiner has not shown that the references contain any language regarding the desirability of the combining the references, as required by M.P.E.P. § 2143.01, *citing In re Mills*, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). Thus, Applicant contends that the disclosure of, motivation, and desirability to make the claimed invention are found only in the instant specification, which evidence cannot be used to satisfy the Office's burden for establishing a *prima facie* case of obviousness. Therefore, for this additional and paramount reason, Applicant respectfully requests that the rejection be withdrawn.

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CONCLUSION

Based on the preceding remarks, Applicant submits that the application is now in condition for allowance, and such action is earnestly requested. As discussed above, Applicant contends that the finality of the rejection should be withdrawn due to the new unsolicited ground of rejection. Should finality not be withdrawn, Applicant requests entry of this response because it will put the application in better condition for appeal.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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